UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,618	12/17/2001	Guido Henning	2001P56011US	1214

28524 7590 08/20/2008

SIEMENS CORPORATION
INTELLECTUAL PROPERTY DEPARTMENT
170 WOOD AVENUE SOUTH
ISELIN, NJ 08830

EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
08/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/022,618	HENNING ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-5,12-14,16 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5, 12-14 and 16-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to the undersigned.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 19 May 2008 has been entered.

3. Claims 1-2, 6-11 and 15 are cancelled.

4. Claims 3-5, 14 and 16-17 have been amended.

5. Claims 3-5, 12-14 and 16-17 are pending and under consideration to the extent of applicant elected inventions, the molecular markers are at least her2/neu and p53 (e.g., reply filed 4/5/05).

6. This Office Action contains New Grounds of Rejections.

Rejections Withdrawn

7. *All rejections in the previous Office Action mailed 9/7/07 are withdrawn in view of the amendments to the claims.*

New Grounds of Objections/Rejections

8. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. For example, see page 5, line 21. Applicants' cooperation is requested in reviewing the entire disclosure for additional embedded hyperlinks and/or other form of browser-executable code that require correction. See MPEP § 608.01.

Claim Rejections - 35 USC 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 3-5, 12-14 and 16-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over McGlynn et al (US Patent 6,005, 256, filed 2/12/1998, IDS reference U2 filed 6/24/02) in view of Hoon et al (U.S. Patent 6,057,105, 12/9/1997) and Pillai et al (Cancer Epidemiology, Biomarkers and Prevention, 1996, 5:329-335, IDS reference R5 filed 12/19/03) and Kihana et al (Cancer, 73:148-153, cited on PTO-892 mailed 6/23/05).

McGlynn et al teach a method and apparatus (e.g., CPU; "diagnostic expert system") for detecting tumor cells in a tissue sample comprising contacting the tissue

sample multiple fluorescent molecular markers (e.g., multiple fluorescently-labelled antibodies), illuminating the sample with one or more excitation wavelengths, simultaneously detecting the emission wavelengths/signals and determining that at least one of the detected signal amplitudes exceed a predetermined threshold level, thereby indicating the presence of tumor cells in the sample (see entire document, particularly cols. 2-6, 10-14 and Figs 4-5 and 12). McGlynn et al do not specifically teach the method for detecting tumor cells in a uterine cervical smear and wherein at least two of the molecular markers are her2/neu and p53. These deficiencies are made up for in the teachings of Hoon et al and Pillai et al and Kihana et al.

Hoon et al teach that detection of individual tumor markers cannot individually detect cancer in a highly specific and sensitive manner due to the high phenotypic diversity found in tumor cells at any one time and during disease progression and detection of multiple markers and marker combinations provide increased sensitivity and specificity for tumor detection and diagnosis (see entire document).

Pillai et al teach a method for detecting tumor cells and their precursors in cervical smears comprising assaying for the presence or absence of p53, HPV-16/-18 E6 and bcl-2 using immunofluorescence microscopy and Pillai et al teach that there is an inverse association between the presence of p53 and invasive cervical disease and the pattern of the presence of high-risk HPV-E6, p53 and bcl-2 proteins may be useful for identifying women at increased risk for the development of invasive cervical cancer, wherein increased amounts of E6 and bcl-2 are associated with high-grade cervical cancer (see entire document, particularly pp. 329, 333-334).

Kihana et al teach the immunoassay of formalin-fixed paraffin-embedded tissue sections of cervical adenocarcinoma for c-erbB-2 protein (her2/neu) which was detected in 77% (34 of 44 cases) of the tumor tissues assayed (see abstract and p. 149, col 1) but only in 13% (1 of 8) of the non-tumor samples tested.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a more sensitive and specific method for detecting tumor cells in a cervical smear comprising contacting the cervical smear multiple fluorescent molecular markers (e.g., multiple fluorescently-labelled

antibodies) that bind to at least her2/neu and p53, illuminating the sample with one or more excitation wavelengths, simultaneously detecting the emission wavelengths/signals and determining that the detected signal amplitude(s) exceed a predetermined threshold level, thereby detecting the presence of cancer cells in the cervical smear.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a more sensitive and specific method for detecting tumor cells in a cervical smear comprising contacting the cervical smear multiple fluorescent molecular markers (e.g., multiple fluorescently-labelled antibodies) that bind to at least her2/neu and p53, illuminating the sample with one or more excitation wavelengths, simultaneously detecting the emission wavelengths/signals and determining that the detected signal amplitude(s) exceed a predetermined threshold level, thereby detecting the presence of cancer cells in the cervical smear in view of McGlynn et al and Hoon et al and Pillai et al and Kihana et al because McGlynn et al teach a method and apparatus for detecting tumor cells in a tissue sample comprising contacting the tissue sample multiple fluorescent molecular markers (e.g., multiple fluorescently-labelled antibodies), illuminating the sample with one or more excitation wavelengths, simultaneously detecting the emission wavelengths/signals and determining that at least one of the detected signal amplitude(s) exceed a predetermined threshold level, thereby indicating the presence of tumor cells in the sample and Hoon et al teach that detection of individual tumor markers cannot individually detect cancer in a highly specific and sensitive manner due to the high phenotypic diversity found in tumor cells at any one time and during disease progression and detection of multiple markers and marker combinations provide increased sensitivity and specificity for tumor detection and diagnosis and Pillai et al teach a method for detecting tumor cells and their precursors in cervical smears comprising assaying for the presence or absence of p53, HPV-16/-18 E6 and bcl-2 using immunofluorescence microscopy and Pillai et al teach that there is an inverse association between the presence of p53 and invasive cervical disease and the pattern of the presence of high-risk HPV-E6, p53 and bcl-2 proteins may be useful for

identifying women at increased risk for the development of invasive cervical cancer, wherein increased amounts of E6 and bcl-2 are associated with high-grade cervical cancer and Kihana et al teach the immunoassay of formalin-fixed paraffin-embedded tissue sections of cervical adenocarcinoma for c-erbB-2 protein which was detected in 77% (34 of 44 cases) of the tumor tissues assayed (see abstract and p. 149, col 1) but only in 13% (1 of 8) of the non-tumor samples tested. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to detect the expression of at least her2/neu and p53 (e.g., her2/neu, p53, E6 and/or bcl-2) since individual tumor markers cannot individually detect cancer in a highly specific and sensitive manner due to the high phenotypic diversity found in tumor cells at any one time and during disease progression and detection of multiple markers and marker combinations provide increased sensitivity and specificity. Thus, it would have been *prima facie* obvious to one skilled in the art to have produced a more sensitive and specific method for detecting tumor cells in a cervical smear comprising contacting the cervical smear multiple fluorescent molecular markers (e.g., multiple fluorescently-labelled antibodies) that bind to at least her2/neu and p53, illuminating the sample with one or more excitation wavelengths, simultaneously detecting the emission wavelengths/signals and determining that the detected signal amplitude(s) exceed a predetermined threshold level, thereby detecting the presence of cancer cells in the cervical smear in view of McGlynn et al and Hoon et al and Pillai et al and Kihana et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by

telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643